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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,168	06/29/2006	Nathalie Norais	PP019737.0004	5751

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

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08/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,168	NORAIS ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *1-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *5-16-05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6-8-09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *tettelin alignment; wang alignment*.

DETAILED ACTION

The response filed 4-23-09 has been entered into the record.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

The information disclosure statement filed 6-8-09 has been considered. An initialed copy is enclosed.

Election/Restrictions

Applicant's election with traverse of Group 582, (claims 9-13) SEQ ID NO:207/NMB1779 in the response filed 4-23-09 is acknowledged. The traversal is on the ground(s) that all the groups now contain the same technical feature and as such have unity of invention. This is not found persuasive because the immunogenic compositions are obvious or anticipated as set forth below and the withdrawn groups do not include all the limitations of group 582, the protein and adjuvant as set forth in the amendment filed 4-23-09. Rejoinder may be considered if all the limitations from any allowable product claims are introduced in the other groups of inventions. Rejoinder is subject to all the

claims in the elected group being allowable. Applicants are reminded that it is incumbent upon applicants to amend the non-elected claims to be commensurate in scope.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 13 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed invention is drawn to a product of nature, a nucleic acid encoding a polypeptide. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a

person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (WO200277183, 03-October 2002) in view of Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pages 53-137, 1989.)

Wang et al teaches a protein encoded by prokaryotic essential gene #13372 (i.e. the nucleic acid). Wang et al teach the nucleic acid of the essential gene. The protein encoded by essential gene #23372 is 99.2% identical as compared with SEQ ID NO:207. The protein of Wang et al has 197 consecutive amino acids in common (residues 1-197).

Wang et al also teach:

"The purified proteins produced from the gene encoding sequences identified as required for proliferation can be used in a variety of protocols to generate useful antimicrobial reagents. In one embodiment of the present invention, antibodies are generated against the proteins expressed from the identified exogenous nucleic acids. Both monoclonal and polyclonal antibodies can be generated against the expressed

proteins. Methods for generating monoclonal and polyclonal antibodies are well known in the art. Also, antibody fragment preparations prepared from the produced antibodies discussed above are contemplated. In addition, the purified protein, fragments thereof, or derivatives thereof may be administered to an individual in a pharmaceutically acceptable carrier to induce an immune response against the protein. Preferably, the immune response is a protective immune response which protects the individual. Methods or determining appropriate dosages of the protein and pharmaceutically acceptable carriers may be determined empirically and are familiar to those skilled in the art."… and

"Antibodies capable of specifically recognizing the protein of interest can be generated using synthetic peptides using methods well known in the art. See, Antibodies: A Laboratory Manual, (Harlow and Lane, Eds.) Cold Spring Harbor Laboratory (1988). For example, 15-mer peptides having an amino acid sequence encoded by the appropriate identified gene sequence of interest or portion thereof can be chemically synthesized. The synthetic peptides are injected into mice to generate antibodies to the polypeptide encoded by the identified nucleic acid sequence of interest or portion thereof. Alternatively, samples of the protein expressed from the expression vectors discussed above can be purified and subjected to amino acid sequencing analysis to confirm the identity of the recombinantly expressed protein and subsequently used to raise antibodies. An Example describing in detail the generation of monoclonal and polyclonal antibodies appears in Example 12." … and

"EXAMPLE 12
Production of an Antibody to an isolated Escherichia coli, Staphylococcus aureus. Enterococcus faecalis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella tvphimurium, Acinetobacter baumannii, Bacillus anthracis, Bacteroides fragilis, Bordetella pertussis, Borrelia burgdorferi, Burkholderia cepacia, Burkholderia forum. Burkholderia mallei. Campvlobacter ejuni, Chlamvdia pneumoniae, Chlamvdia trachomatis, Clostridium, acetobutvlicum, Clostridium botulinum, Clostridium difficile, Coanebacterium diptheriae, Enterobacter cloacae, Enterococcus faecium, Haemophilus influenzae, Helicobacter pvlori, Leionella pneumophila. Listeria inonocytoze ycobacteriuln bovis, Mvcobacterium leprae. Mvcobacterium tuberculosis. Mcoplasma genitalium. Mvcoplasma pneumoniae, Neisseria gonorrhoeae, Neisseria Meningitidis, Pasteurella multocida, Proteus mirabilis, Pseudomonas putida, Pseudomonas syringae, Salmonella paratvplti, Salmonella tvphi, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus mutans, Staphylococcus pneumoniae, Staphylococcus pyogenes, Treponema pallidum, Ureaplasma urealyticum, Vibrio cholerae or Yersinia pestis Protein Substantially pure protein or

polypeptide (including one of the polypeptides of SEQ ID NOs.: 42398-78581) is isolated from the transformed cells as described in Example 11. The concentration of protein in the final preparation is adjusted, for example, by concentration on a 10,000 molecular weight cut off AMICON filter device (Millipore, Bedford, MA), to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows: Monoclonal Antibody Production by Hybridoma Fusion Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., Nature 256: 495 (1975) or any of the well-known derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody-producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells are destroyed by growth of the system on selective medium comprising aminopterin (HAT medium). The successfully-fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as described by Engvall, E.,"Enzyme immunoassay ELISA and EMIT," Meth. Enzymol. 70: 419 (1980), and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. Basic Methods in Molecular Biology Elsevier, New York. Section 21-2.
Polyclonal Antibody Production by Immunization Polyclonal antiserum containing antibodies to heterogeneous epitopes of a single protein or a peptide can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than larger molecules and can require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al. J. Clin. Endocrinol. Metab. 33: 988-991 (1971). Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: Handbook of Experimental Immunology D.

Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 1). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: Manual of Clinical Immunology, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D. C. (1980). Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies can also be used in therapeutic compositions for killing bacterial cells expressing the protein."

While Wang et al teaches immunogenic compositions comprising the proteins or at least 15 mers thereof in compositions with pharmaceutically acceptable carriers. Wang et al teaches that the protein immunization can be unmodified or modified to enhance immunogenicity by use of carriers and an adjuvant. Wang et al differs by not explicitly teaching the protein or 15-mer together with an adjuvant.

Harlow et al teaches conventional means of forming immunogenic compositions including the use of adjuvants and carriers to stimulate an immune response as a matter of routine cited by Wang et al (see Chapter 5 and for example 76, 77 and 96),

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the protein or 15-mer derived there from of Wang et al with an adjuvant in order to make antibodies according to Wang et al because Harlow et al and Wang et al teach that adjuvants can boost the immune response to protein antigens.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (WO200277183, 03-October 2002) and Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pages 53-137, 1989) as applied to claims 9-11 and 13 above and further in view of Telford et al (WO 02/34771, May 2, 2002)

The combination of Wang et al in view of Harlow and Lane is set forth surpa. The combination differs by not placing the protein or peptide of the prior art in a hybrid protein multimer having the formula of NH2-A-[-X-L-}n-B-COOH in an immunogenic composition.

Telford et al teach Streptococcus peptides and proteins in the formula of NH2-A-[-X-L-}n-B-COOH. See in particular page 5, line 19 to page 9 in an immunogenic composition comprising the adjuvant aluminum. Immunogenic compositions comprising the proteins including the hybrid protein are described at page 22, lines 6-24). Telford et al teaches that the hybrid protein formula provides for leader sequences to direct protein trafficking, facilitate cloning and purification (page 5, lines 19-34).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to make a homomultimer of the full length protein or 15-mer peptides of Wang et al according to the formula of Telford et al and substitute the hybrid homomultimeric protein/peptide for the monomeric protein/peptide in the composition as combined *surpa* because Telford et al teach that the hybrid proteins of that formula are useful in immunogenic compositions. It would have been *prima facie* obvious to make the hybrid protein by recombinant DNA means as the hybrid formula provides for sequences that facilitate cloning and protein leader sequences to direct protein trafficking or short peptide sequences which facilitate purification.

Claims 9-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tettelin et al (Science, 287:1089-1805, 2000; of record on 1449) in view of Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pages 53-137, 1989) and Campbell (Monoclonal Antibody Technology, Chapter 1 pages 1-32, Elsevier Science Publishing Company, Inc., 1986, section 1.3.4).

Tettelin et al teach the polypeptide having accession number NMB1799. NMB1799 is 100% identical as compared with SEQ ID NO:207 (see attached sequence comparison).

Tettelin et al differ by not placing the protein in an immunogenic composition with an adjuvant.

Harlow et al teaches conventional means of forming immunogenic compositions including the use of adjuvants and carriers to stimulate an immune response to an antigen as a matter of routine preparation of immunogenic compositions for making antibodies (see pages 35-137).

Campbell teaches that "It is customary now for any group working on a macromulecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application." (page 29, section 1.3.4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to combine the polypeptide NMB1799 of Tettelin et al with an adjuvant to form an immunogenic composition for making antibodies because Campbell et al teaches that it is customary for making monoclonal antibodies to macromolecules even without a clear objective for the application of the monoclonal antibody.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tettelin et al (Science, 287:1089-1805, 2000; of record on 1449), Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pages 53-137, 1989) and Campbell (Monoclonal Antibody Technology, Chapter 1 pages 1-32, Elsevier Science Publishing Company, Inc., 1986, section 1.3.4) as applied to claims 9-11 and 13 above and further in view of Telford et al (WO 02/34771, May 2, 2002).

The combination of Tetelin et al, Harlow et al and Campbell is set forth *supra*. The combination differs by not placing the protein of the prior art in a hybrid protein multimer having the formula of NH2-A-[-X-L-}n-B-COOH in an immunogenic composition.

Telford et al teach Streptococcus peptides and proteins in the formula of NH2-A-[-X-L-}n-B-COOH. See in particular page 5, line 19 to page 9 in an immunogenic

composition comprising the adjuvant aluminum. Immunogenic compositions comprising the proteins including the hybrid protein are described at page 22, lines 6-24). Telford et al teaches that the hybrid protein formula provides for leader sequences to direct protein trafficking, facilitate cloning and purification (page 5, lines 19-34).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to recombinantly make a homomultimer of the full length protein of Tettelin according to the formula of Telford et al and substitute the hybrid homomultimeric protein/peptide for the monomeric protein/peptide in the composition as combined *surpa* because Telford et al teach that the hybrid proteins of that formula are useful in immunogenic compositions. It would have been *prima facie* obvious to make the hybrid protein by recombinant DNA means as the hybrid formula provides for sequences that facilitate cloning and protein leader sequences to direct protein trafficking or short peptide sequences which facilitate purification.

Status of the Claims

Claims 9-13 stand rejected. Claims 1-8 are withdrawn from consideration.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor Robert Mondesi can be reached at 571-272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia A. Duffy/
Primary Examiner